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Title: An Etiology for Medication Ordering Errors in CPOE Systems

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In this final report, we summarize the background, methodology, results, and lessons learned from our AHRQ R21 observational study on the void function. We also summarize related sub-projects and findings based on the data collected as part of this work. Finally, we highlight the publications, and implementation products that resulted from this work.

STUDY BACKGROUND

Medication errors cause adverse drug events (ADE) in nearly 5% of the inpatient population [1]. Although significant research on computerized provider order entry (CPOE)-related medication errors exists (e.g., [2, 3]), errors that occur during the medication ordering stage are minimally explored [4, 5]. Consequently, our current understanding of medication ordering errors are primarily based on retrospective methods using case studies [6, 7], chart reviews [8, 9], malpractice claims [10], and self-reported incidents [11-13]. However, these error-reporting methods have been critiqued for their voluntary, non-verifiable, cumbersome and time-consuming format [14-16], contributing to the under-reporting of ordering errors [11-13].

Based on prior research [17-19], we identified and leveraged a CPOE-integrated function [20] referred to as "void" as a potential approach to report and intercept medication ordering errors. Using this function, clinicians can identify and remove a medication order placed in error within their ordering workflow. Additionally, clinicians can also report on the type of medication ordering error (including duplicate, wrong patient, wrong drug).

STUDY METHODOLOGY

Study Setting, Sample and Participants

This study was conducted at a tertiary academic medical center. Only inpatient orders written in the 495-bed hospital were included. Medication orders were placed using a CPOE (Cerner Powerchart®) with clinical decision support (CDS) features for drug-drug interactions, drug-laboratory, drug-diet, drug-disease and duplicate order alerts. Inpatient orders for the adult and pediatric populations that were voided over a 16-month study period (August 25, 2017–December 31, 2018) were included.

Study participants included *ordering* clinicians (i.e., those placing an inpatient medication order that was subsequently voided) and *voiding* clinicians (i.e., those identifying and intercepting an inpatient medication ordering error). Ordering and voiding clinicians included physicians, nurses, pharmacists and medical students. Nurses and pharmacists placed orders based on verbal and protocol-driven orders from physicians.

Data Collection

Training and Recruitment

Prior to the start of the study, an email that included a "Job Aid" describing the purpose and how to use the medication void function was sent to all hospital employees with ordering capabilities. For new employees, this information was included as part of their training materials (*see* Appendices S2, S3).

Void Alert Tool Triggers

To prospectively identify voided orders placed in inpatient settings, a void alert tool (VAT) was developed. When an order was voided, the VAT triggered a secure email containing details of the voided order to the researchers' clinical inbox. Upon receiving this email, relevant information from the patient's

chart regarding the order (e.g., patient, clinician, order, and medication characteristics), and the clinician-selected type of ordering error (referred to as "Clinician-CPOE-selected") was documented in the REDCap study database.

Follow-up Interviews and Surveys

Within 24 hours of a VAT trigger, clinicians (both ordering and voiding clinicians) were contacted using the hospital's paging system. A researcher followed-up with interviews of ordering and voiding clinicians who responded and verbally consented for participation before beginning the interview. The interview questions were guided by our pilot research [18] and similar research studies on medication errors [5, 21, 22]. To further investigate the risk factors to medication ordering [5, 23], interview questions were based on the SEIPS (Systems Engineering Initiative for Patient Safety) model [24]. The SEIPS model helps elucidate the elements of the medication ordering work system, including people (e.g., clinicians), their tasks (e.g., medication ordering), tools and technologies (e.g., CPOE system), physical environment (e.g., clinical unit), and organizational aspects (e.g., protocols) and their interdependencies which can impact the medication ordering process and its related outcomes (e.g., near miss, ADE) [25]. Interview questions focused on the specific ordering error, its type (referred to as "clinician-reported" type of ordering error), SEIPS-based risk factors (e.g., technological, social, cognitive) that contributed to the errors, and error-mitigation strategies to prevent the ordering error under inquiry. All interviews were audio-recorded and lasted approximately 10 minutes. We also followed-up with web-based surveys sent via REDCap as a secure link for those clinicians who could not be reached via pagers.

Chart Reviews

Chart reviews are often considered as the basis for establishing the "ground truth" and a reliable and validated method for ascertaining errors and adverse events. Towards this end, we conducted chart reviews on VAT-triggered orders to: (a) evaluate whether a voided order was an actual medication ordering error, (b) identify the true type of ordering error (referred to as "chart review-based" type of ordering error); (c) verify whether the clinician-CPOE-selected or clinician-reported type of ordering error aligned with the chart review-based type of ordering error; and finally, (d) ascertain whether the ordering error had an impact on patient safety.

To assess the chart review-based type of medication ordering errors, and categorize its impact as a near miss (i.e., no harm) or ADE (i.e., harm), we used a validated framework (Table 1) derived from our previous studies [18, 19] and an abridged taxonomy developed by the NCC MERP [26] respectively. A chart abstraction tool was developed to extract chart information.

Table 1. Types of medication ordering errors, and their descriptions.

Types of Medication Ordering Errors	Description of Ordering Error
Duplicate Order	An identical order to one already active in the list of medications.
Not Clinically Appropriate	An order that was cancelled rapidly, or prior to administration without an indication noted in the patient chart.
Wrong Encounter	An order placed on the incorrect patient encounter episode that causes it to be non-actionable for the intended care of the patient.
Wrong Patient	An order indicating that the medication was placed on the wrong patient.
Wrong Route/Dose/ Schedule/Strength	An order indicating an error in the construction of the order: route, dose, schedule, or strength.
Wrong Drug	An order indicating the wrong medication for the patient.

Data Analysis

Interviews and surveys were analyzed using a structured coding approach informed by the SEIPS model. Any additional data captured using the 'other' category for the risk factors and error mitigation strategies were openly coded [27]. After coding, a thematic analysis [28] was performed to identify patterns across clinician responses based on similarities. Our primary measure was the positive predictive value (PPV) of the true medication ordering errors among the voided orders. Descriptive characteristics of erroneous orders including clinician, patient and order were generated.

We treated the medication ordering errors that resulted in near misses and adverse events as categorical variables and presented them as frequency and proportion. We also compared the overlap between the clinician-CPOE-selected, clinician-reported, chart review-based types of medication ordering errors. All analyses were conducted using R version 3.4

OVERALL SUMMARY OF FINDINGS

1074 voided orders triggered the VAT during the 16-month study period. All voided orders were followed-up with interviews or surveys and chart reviews. We also conducted 387 interviews/surveys on 355 (33% response rate) orders with 286 clinicians.

Aim 1: To investigate clinician provided reasons for CPOE-based medication voiding.

Type of Medication Ordering Errors

Based on chart review-based classification of error types, the most prevalent ordering errors were duplicate orders (51%, n=423), wrong route/dose/schedule/strength orders (22%, *n*=189), wrong patient (11%, *n*=94), not-clinically appropriate (7%, *n*=64), wrong drug (7%, *n*=56), wrong encounter (1%, *n*=11), or other (<1%, *n*=5).

Based on clinician-CPOE-selected type (i.e., at the time of order), the most common ordering errors were duplicate (52%), wrong route/dose/schedule/strength orders (21%), other (13%), ordered on the wrong patient (11%), or wrong encounter (3%). Compared to the chart review-based error type, we found that clinician-CPOE-selected and chart review-based type of medication errors were the same in over 80% of the medication errors (PPV=80.3±1.5%).

268 of 355 orders (75%) with interviews/surveys were true medication ordering errors based on chart review. 286 clinicians responded to interviews/surveys (176 physicians, 35 pharmacists, 45 nurses, 30 belonging to "other" category (e.g., Doctor of Dental Surgery and medical students).

Based on clinician-reported type (i.e., at the time of interview), the most common medication ordering errors were duplicate (32%), wrong route/dose/schedule/strength (20%), not clinically appropriate (10%), or ordered on the wrong patient (9%).

AIM 2: To identify medication ordering errors from voided orders, and their clinical impact.

Medication Voiding and Ordering Errors

Our chart reviews confirmed that 842 (of 1074) voided orders were true ordering errors (PPV=78.3±1.2%). These errors were primarily generated by physicians (63%) and originated in intensive care or step-down units (38%), other (21%), surgery (17%), medicine wards (14%) or labor & delivery (7%). Similarly, ordering errors were intercepted (i.e., voided) primarily by physicians (54%), pharmacists (20%) or nurses (20%). The median time from medication ordering to its voiding was 0.38 hours (Table 2).

Table 2. Characteristics of medication ordering errors identified using void orders. *other category for the encounter location included short stay unit, psychiatry, rehabilitation unit; **other category for clinician-selected (CPOE) error type was one of the CPOE void drop-down choices available at the time of voiding; ***other category for clinician-reported (interview) type included medical student order, contraindicated orders, orders not relevant anymore for patients; ****other category for chart-review based type referred to instances where the ordering error type could not be determined.

Variable(s)	Value
Patient Age, Mean (SD)	48.9 (20.9)
Patient Sex (=Female)	458 (54.4%)
Median Time to Void	0.38 hours
Encounter Type, n(%)	
Inpatient	822 (97.7%)
Missing	20 (2.3%)
Encounter Location, n(%)	
ED	7 (0.8%)
ICU	318 (37.8%)
Medicine Wards	119 (14.1%)
OB/Labor & Delivery	58 (6.9%)
*Other	180 (21.4%)
Pediatrics	18 (2.1%)
Surgery	136 (16.2%)
Missing	6 (0.7%)
Ordering Clinician Role, n(%)	
MD	525 (62.3%)
Nursing	160 (19.0%)

Variable(s)	Value
Ordering Clinician Role, n(%)	
PharmD	49 (5.8%)
Other	97 (11.5%)
Missing	11 (1.3%)
Voiding Clinician Role, n(%)	
MD	451 (53.5%)
Nursing	174 (20.6%)
PharmD	162 (19.2%)
Other	49 (5.8%)
Missing	6 (.7%)
Orderer/Voider=SAME	504 (59.8%)
Clinician-selected type (CPOE), n(%)	
Duplicate Order	434 (51.5%)
Improperly Composed Order	173 (20.5%)
Incorrect Ordering Physician	8 (0.9%)
**Other	110 (13.1%)
Wrong Encounter	23 (2.7%)
Wrong Patient	94 (11.1%)
Clinician-reported type (interview), n(%)	
Duplicate	86 (31.9%)
Not Clinically Appropriate	26 (9.6%)
***Other	48 (17.8%)
Wrong Drug	17 (6.3%)
Wrong Encounter	4 (1.4%)
Wrong Patient	23 (8.6%)
Wrong Route/Dose/Strength	54 (20.0%)
No Reason Reported	11 (4.1%)
Chart review-based type, n(%)	
Chart review-based type	423 (50.2%)
Not Clinically Appropriate	64 (7.6%)
****Other	5 (0.5%)
Wrong Drug	56 (6.6%)
Wrong Encounter	11 (1.3%)
Wrong Patient	94 (11.1%)
Wrong Route/Dose/Strength	189 (22.5%)

Impact of Medication Ordering Errors on Safety

No ADEs were identified among the ordering errors. 78% (*n*=652) of the medication ordering errors (i.e., near misses) were intercepted prior to administration, and did not reach the patient (i.e., near miss error, no harm, *did not* reach patient); 22% (*n*=190) were intercepted after at least a single medication administration (i.e., near miss error, no harm, *reached* patient).

Aim 3: To develop statistical and descriptive models for characterizing medication ordering errors.

Clinician-Reported Risk Factors Associated with Medication Ordering Errors

Using the SEIPS model, risk factors associated with errors were classified into technological, cognitive, social, environmental and organizational. A summary of the sub-factors associated with each is illustrated in Figure 1. The most important sub-factors associated with each risk factor are described in the sections below.

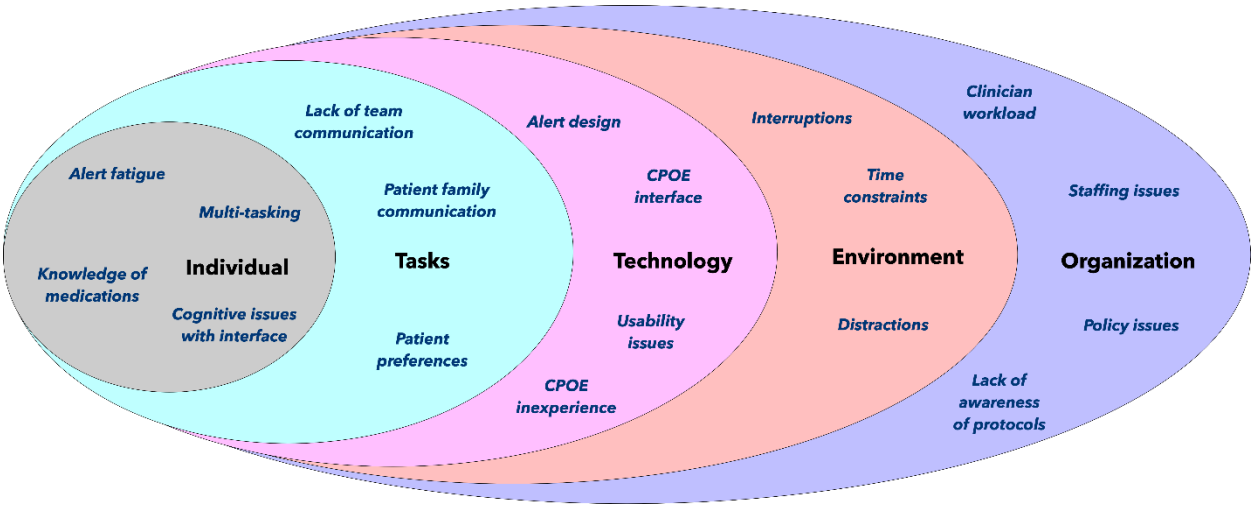


Figure 1. SEIPS-based risk factors associated with medication ordering errors.

Among the considered factors, the technological and cognitive factors were the most common risks contributing to all ordering errors. In particular, technological factors were the primary contributors to duplicate and wrong encounter type of errors, while cognitive factors predominantly contributed to wrong drug, wrong patient and wrong route/dose/schedule/strength errors (Table 3). However, all risk factors were associated, to some degree, with each of the types of errors. In the following sections, we highlight how each of these risk factors manifested in medication ordering errors.

Table 3. SEIPS-based risk factors associated with each type of medication ordering error; each cell shows the proportion of the contribution of each risk factor for a medication error type.

	Technological Factors	Cognitive Factors	Social Factors	Environmental Factors	Organizational Factors
Duplicate Order	0.40	0.23	0.24	0.09	0.04
Wrong Drug	0.30	0.48	0.00	0.12	0.10
Wrong Encounter	0.50	0.00	0.50	0.00	0.00
Wrong Patient	0.19	0.51	0.01	0.18	0.11
Wrong route/dose/schedule/strength	0.29	0.36	0.10	0.12	0.13
Not Clinically Appropriate	0.40	0.20	0.33	0.00	0.07
Other	0.43	0.19	0.19	0.06	0.13

Technological Risk Factors

Frequently-reported technological risk factors included CPOE interface design (16% of clinician-reported technological risk factors) and usability issues arising from "a *confusing EHR (MD-894; we use the format"Clinical Role-Void ID"),"* CDS alert design issues (12%), and limited CPOE training/experience (16%). CPOE usability issues (38%) slowed the system response during order verification and modification steps. This was partly attributed to the overwhelming number of menu choices during ordering that resulted in either missed clicks or inattentive clicking. A clinician commented that "*there's more clicking barriers... and clicking fatigue sometimes gets in the way*" (*MD-912)* of ordering. Dissimilarities in the CPOE user interface views across physicians and nurses created bottlenecks due to limited awareness about patient orders and their status. CPOE alert notifications were often indirect and lengthy*:"The pop-up really didn't give me the best information. It was a confusing message…." (388-APN)*, with generic information as highlighted: "*EHR-CPOE is unable to read its own history and apply relevant info to new orders or alert when ordering*" (*MD-75*). Senior clinicians attributed their trainees' inexperience with the CPOE system for ordering errors, meanwhile trainees expressed concerns about the inadequate CPOE training: *"Poorly taught,… modules are not effective teaching tools in my opinion" (MD-894).* The initial training provided was short (~3 hours) and often forgotten: "*orientation was 2 months ago and we only had 1 hour Cerner course and I didn't remember... by the time I got to use Cerner for the first time, I couldn't remember anything from the hour of orientation*" (*MD-844*).

Cognitive Risk Factors

In addition to the commonly reported cognitive risk factors related to multitasking (15%), alert fatigue (10%), other distinct risk factors included clinician negligence (29%), misinterpretation of verbal orders (4%), and mix-up of patient charts (6%). Clinician negligence caused by inattention to ordering details and limited review and verification of medication lists at the time of ordering was associated with ordering errors. Similarly, verbal orders were often misunderstood or misinterpreted. Some of the misunderstandings or misinterpretations were attributed to workflow interruptions from multiple verbal order requests: "*Putting order on multiple patients in a clinical setting where you are running around physically having to do things and having to come back to it to place orders*" (*MD-466*). Finally, clinicians mixed-up patients with similar diagnois/problem lists and treatments: *"There was another patient who needed insulin and their medical records are similar with similar medications ordered for them" (MD-156).*

Social Risk Factors

Frequently referenced social risk factors included communication gaps among clinicians (53% of social risk factors) and between clinicians and patients or their caregivers (47%). Errors attributed to social factors arose as a result of clinicians' limited awareness about modified patient therapy or care plan changes. This example illustrates how a clinician ordered the medication, without realizing updates in patient status: *"There was the expectation that by the time the next dose is going to be needed, he will no longer be NPO, but then they were unable to deescalate care as anticipated" (MD-221).* Communication gaps about medications were also persistent during care transition periods including morning rounds and handoffs: "*miscommunication between the person who was here for 24 hrs and was leaving and the people taking over*" (*MD-965*). Limited clinician communication with patients or caregivers about home medication lists and medication use history (e.g., patient preferences) also led to errors: "*it was just due to discussion with the patient,"* that the clinician established *"what* [medication] *would be best for her*" (*RN-200*).

Environmental Risk Factors

Commonly reported environmental risk factors included interruptions (42% of environmental risk factors), distractions (30%), noise (14%), and time constraints within the environmental context (2%). Interruptions from pagers and alarms were disruptive as emphasized by a clinician who was frequently "*getting interrupted by pages" (MD-959),* while ordering medications or getting distracted while multitasking or due to noise (e.g., beeping sounds from alarms). Some clinicians felt considerable time pressure and rushed through the ordering process where they were *"trying to do things too quickly for a patient" (MD-707)* resulting in erroneous orders. Due to time constraints, clinicians failed to review active medication lists, verify orders, or leave special instructions for unique orders. Alternatively, the lack of thoroughness with original orders was also attributed to the potential oversight and verification by pharmacists: "*I was in a hurry and was not careful and I know that I can always delete an order.. [after pharmacy review]" (APN-997).*

Organizational Risk Factors

Organizational risk factors included high clinician workload (61% of organizational risk factors), staffing issues (14%), limited protocol awareness (11%), and protocol violations (10%). High clinician workload led to limited order verification and review of critical alerts. A clinician stated: "*my workload is such that I often do not have enough time to look things up before I order them..." (MD-828)*. Another clinician further added that the workload introduced "*a lot of stress…*" (*MD-844*). Limited staffing led to clinicians often assuming temporary clinical responsibility for patients not usually under their care resulting in errors due to limited knowledge about the patients' medications or their clinical trajectory. Limited awareness of policies and violations from unit-based and institution-based medication ordering protocols were associated with errors. A nurse commented about a protocol violation where a verbal order was given for a high-risk, high-alert medication: *"I don't usually put in prescription, it was a protocol… [when I did] I got a duplicate alert. It is a high risk medication" (RN-571).* Other cases of policy violations were reported by clinicians placing orders to verify insurance coverage for the medication by the pharmacy: *"an erroneous policy in which the pharmacy cannot tell you what is covered unless you prescribe it first. I think that's a bad policy" (MD-705).* Similarly, incorrect order entries were used as a workaround to get pharmacists to verify medication orders.

Clinician-Reported Strategies for Mitigating Errors

Clinicians suggested several strategies to mitigate errors and their associated risk factors. Clinicians emphasized that there should be a deliberate cognitive effort from ordering clinicians to verify the active medication lists of patients as part of their routine CPOE-ordering workflow. Furthermore, many clinicians proposed several modifications to improve design and usability of the CPOE-CDS system interface including restricting easy flipping between charts, highlighting duplicates at the time of ordering both within the order set and within individual orders, enhancing readability of medication ordering summary, rephrasing CDS alert narratives and applying precise wording for order sentences. Lastly, clinicians called for implementing new ordering and communication protocols to add another layer of safety, improving protocol awareness, and building and sustaining ongoing CPOE enrichment and training efforts. Please see detailed list in Table 4.

Table 4. Clinician-Reported strategies for mitigating medication ordering errors and their risk factors.

Clinician-Recommended Strategies	
Duplicate Ordering Errors	
Clinician-level	• Review medication lists prior to ordering (prompt to review) • Refresh order entry page before finalizing orders
CPOE-CDS-level	• Prevent easy chart flipping • Improve wording of CDS alerts and order sets • Create "true" duplicate alerts and review prompts • Update CPOE instantly to minimize lag time • Block simultaneous order entries by multiple clinicians • Allow clinicians to modify order sets and highlight duplicates with order sets/individual orders • Generate and run ordering report for patient at time of ordering • Organize medication summary more clearly to increase readability • Increase visibility of order set medications
Unit- and Organizational-level	• Increase training and orientation on eMAR (electronic medication administration record) and CPOE shortcuts and menu options; drug-ordering policies, common drugs, and ordering workflow within CPOE (especially for interns), and offer ongoing enrichment classes • Minimize or eliminate verbal orders • Implement standardized communication protocols • Increase number of providers (e.g., interns) in practice
Wrong Dose/Route/Strength	
Clinician-level	• Allow access to home medication list • Review and verify special orders
CPOE-CDS level	• Limit order options based on current medication availabilities at pharmacies • Create pre-saved order sets for future access (including for special unit orders) • Show all applicable order routes at time of ordering • Improve interoperability between eMAR and CPOE • Create concise order sentences in CPOE • Color-code medication routes • Design flags for one-time orders vs. continued orders • Set reminder pop-ups on specific types of dosages • Create customizable alerts based on clinician ordering behaviors/ contextual patterns • Develop a CPOE-based error recognition/prediction system to alert clinicians of potential common ordering mistakes (e.g., pharmacy decision support) • Condense all order information on one tab to minimize clicks and tab switching • Update search feature on orders • Automatically cross-reference insurance policies with medication options • Automatically calculate medication costs before ordering
Clinician-Recommended Strategies	

Wrong Dose/Route/Strength	
Unit- and Organizational-level	• Increase training and orientation on drug-ordering policies, common drugs, and ordering workflow within CPOE (especially for interns) • Develop a formal communication channel between provider and pharmacist via CPOE to place correct order • Add a required protocol step to check medication and dosing before ordering
Wrong Patient	
Clinician-level	• Read the patient first and last Name and double check the chart at time of ordering • Review the order entry before signing
CPOE-CDS level	• Make patient name noticeable on order page (color, italics) • Allow clicking of only relevant ordering options • Use additional patient identifiers (first and last name, location, problem lists etc.) when communicating verbal orders
Unit- and Organizational-level	• Increase training on eMAR
Wrong Drug	
Clinician-level	• Communicate with patient about preferences prior to medication reconciliation • Set up fatigue protocol to review actions for errors • Include medication indication checklist for handoffs • Review medication list at time of ordering
CPOE-CDS level	• Display primary care provider and patient-preferred pharmacy at time of ordering
Unit- and Organizational-level	• Wait to place postoperative orders after patient admission to postoperative units • Improve protocol on time management and task attentiveness • Training on protocols for special medications (opioids, brain toxic meds, methadone program)
Wrong Encounter	
CPOE-CDS level	• Label encounters to be more noticeable on display

Lessons Learned and Conclusions

Clinicians used the CPOE-based void function to intercept and report different types of ordering errors. 22% of the ordering errors reached the patient, albeit without patient harm, highlighting the utility of such tools for capturing medication ordering errors within the clinician ordering workflow. Furthermore, clinicians used the void function to accurately select the appropriate type of medication ordering error 80% of the time, demonstrating its potential broader value in creating a robust taxonomy of errors.

Using the SEIPS model, we ascertained that each ordering error type had a combination of associated risk factors within the ordering work system as opposed to being associated with individual risk factors, highlighting the need for a holistic multi-level approach for potentially mitigating them. In other words, although a specific risk factor may be a predominant contributor, the causal underpinnings for errors can be identified only with such a macro-ergonomic, human-centered approach. With this approach, we

extend previous research that has primarily examined isolated factors contributing to ordering errors (mostly technological barriers and their unintended consequences) [29].

Duplicate orders and wrong route/dose/schedule/strength orders contributed to majority of the ordering errors, and all ordering errors had underlying technological and cognitive risks factors, as previously shown [23, 30]. For example, duplicate ordering errors were attributed to technological risk factors associated with ambiguous EHR-generated medication lists, and inaccurate duplicate order alerts triggered for order renewals, modified doses, creating a nuisance that decreased the likelihood of heeding to a "true" duplicate alert [5]. Similarly, wrong route/dose/schedule/strength errors were linked to cognitive factors, particularly due to loss of attention and limited knowledge about the correct dose, schedule, strength and route for all formulary medications [31].

Currently mitigation strategies to address these various ordering errors have centered around implementing technological fixes [32, 33] such as the wrong-patient retract-and-re-order alerts [34], problem-based indication alerts [35-37], Tall Man lettering [38, 39], grouped alerts [40], use of patient photographs when ordering [34], restricting number of open-charts [41], and use of template order sets and sentences [42, 43]. Despite the efforts, such technological fixes are minimally effective in significantly reducing medication errors [37, 41, 44-46]. Therefore, in order to create a medication safety promoting "balanced work system," the our study emphasizes the need for a multi-level approach targeted at the individual clinician-, CPOE-CDS technology-, and the clinical unit- and organizational- levels to accounting for the ordering work system elements and their interdependencies.

This study underscores the implications of the void function for both research and practice. *First*, the void function offers a practical yet standardized method to collect and create a rich source (or large database) of the different types of medication ordering errors for future research and learning opportunities. *Second*, the void function can potentially increase reporting of ordering errors by clinicians and contribute to our empirical evidence on ordering errors. In particular, it addresses some of the key limitations of current error-reporting methods [30, 47, 48]. As demonstrated by our findings, the void function is straightforward and user-friendly, requiring minimal clinician effort to accurately capture and document the error type, and is able to document even routine and unbiased errors that are near misses (that are never captured in any retrospective error reporting methods), but are nevertheless errors. Such a database can be invaluable for medication and patient safety officers and can also serve as a training platform. *Finally*, utilizing such error reporting functions within the CPOE system and ordering workflow will allow not only standardized collection and documentation of errors but also standardized exchange of error data with national patient safety organizations to develop translational medication safety practices and policies. Such a collaborative exchange of erroneous data from institutions across the nation with safety organizations will help us to build and implement a sustainable "medication safety learning healthcare system" where we can learn from each other's errors and near misses, while promoting rapid innovation and change at the system level, not just with technological solutions [49, 50].

Medication errors represent between the fourth and sixth leading cause of death in the United States [51], a significant public health threat [52]. Medication ordering errors are prevalent [53], are particularly hard to capture and hence have been under-reported. We leverage a CPOE-based void function that can be utilized for reporting and intercepting errors during clinician ordering workflow. In this paper, we report on the different types of ordering errors documented by clinicians using the void function, the underlying risk factors associated with those errors within the medication ordering work system, and the need for multi-faceted strategies for ensuring medication ordering safety.

ADDITIONAL ANALYSIS RELATED TO THE AHRQ R21 STUDY

Predicting Medication Ordering Errors from Contextual Medical Information*:* Objective: Current approaches to understanding medication ordering errors rely on relatively small error samples captured using retrospective reviews or observational studies. These are resource-intensive, do not scale to large computerized provider order entry (CPOE) systems, and are likely to miss important predictors of errors. We investigated the potential for machine learning (ML) models to predict erroneous medication orders and identify contributing factors. Materials and Methods: Erroneous medication orders were captured using a CPOE-based medication voiding function over 6 years. We retrieved patient demographics (race/ethnicity, sex, age), clinician characteristics, type of medication order (inpatient, prescription, home medication by history), and order content. We fit logistic regression models, multiple tree-based ML models, and artificial neural networks. Model performance was evaluated using area under the receiver operating characteristic curve (AUROC) and the area under the precision-recall curve (AUPRC). Results: The dataset included 5,804,192 medication orders, of which 28,695 (0.5%) were voided. ML correctly classified voids at reasonable accuracy; with a positive predictive value of 10%, ~20% of errors were included. Gradient boosted decision trees achieved the highest AUROC (0.7968) and AUPRC (0.0647) among all models. Logistic regression had the poorest performance. Models identified predictive factors with high face validity (e.g., student orders), and a decision tree revealed interacting contexts with high rates of errors. Discussion and conclusion: Automated prediction models using order-entry information offers promise for error surveillance, patient safety improvements, and targeted clinical review. The improved performance of models with complex interactions points to contextual information as important to understanding CPOE errors.

Effects of CPOE on Outcomes*: An Overview of Systematic Reviews:* Background: Computerized provider order entry (CPOE) systems are widely used in clinical settings for the electronic ordering of medications, laboratory tests, and radiologic therapies. However, evidence regarding effects of CPOE use on clinical and safety outcomes has been mixed. We conducted an overview of systematic reviews (SR) to characterize the cumulative effects of CPOE use on outcomes. Method: MEDLINE, EMBASE, CINAHL, and the Cochrane Library were searched to identify published SRs from inception to February 12, 2018. SRs investigating the effects of the use of CPOE were included. Two reviewers independently extracted data and assessed the methodological quality of included SRs. Results: 7 SRs were included for review. Less than 7% of the 118 studies included in the SRs were RCTs. Pooled studies from the SRs in inpatient settings showed that CPOE use resulted in statistically significant decreases in medication errors and adverse drug events; however, there was considerable variation in the magnitude of their reduction (54-92% for errors, 35-53% for ADEs). There was no significant effect on hospital mortality or length of stay. Bibliographic analysis showed limited overlap (24%) among studies included across all SRs. Conclusion: SRs on CPOEs included predominantly non-RCTs and observational studies with varying review foci highlighting limited duplication in research efforts. However, there was significant heterogeneity across the SRs due to variations in the comparison groups and definitions of the considered outcomes. With 5 of the 7 SRs having low to moderate quality, findings may have overestimated the true CPOE effects. Future SRs should adhere to methodological guidelines and improve their reporting characteristics.

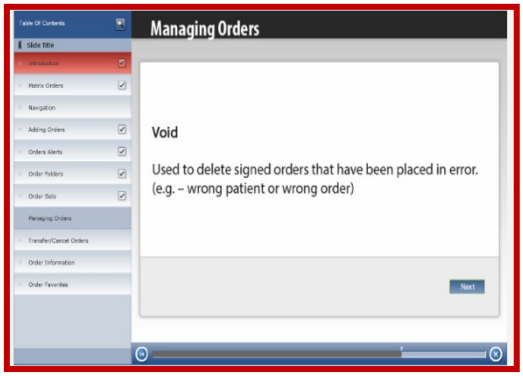
Analysis of High-Risk Medications among Medication Ordering Errors: Objective: To investigate whether medications present on the Institute for Safe Medication Practices (ISMP) List of High Alert Medications in Acute Care Settings (List) were more likely to be voided, when accounting for other potential confounders. Methods: This study was conducted at a tertiary academic medical center. All inpatient orders written between August 25, 2017 and December 31, 2018 were included in the analysis.

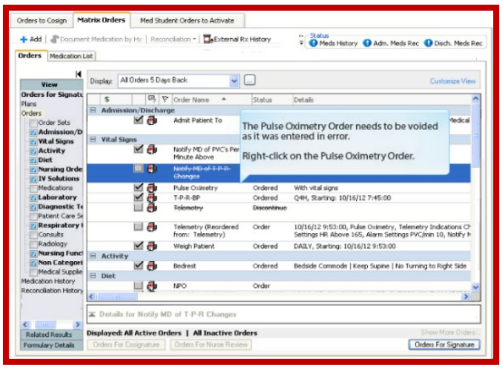
Voided medication orders were identified through a report generated through the medical center's electronic health record and linked to the medication order. Medications identified being on the ISMP List was entered into a multivariate logistic regression model as the independent variable. Additional variables considered for inclusion in the model were classification as IV fluid, anticoagulant, benzodiazepines, chemotherapy, opioid, or vaccine. Other covariates considered for inclusion were prescriber type (physician, resident, study, nurse, pharmacist, or other), location of patient (ICU, labor and delivery, medical/surgical, pediatric ICU, or psychiatry), route (several considered), and shift (day, evening, or overnight). Model covariates were considered for inclusion in the model if they were associated the dependent variable (medication voided) in univariate analyses with a $p < 0.2$. Covariates were entered into the model using a forward stepwise approach. All covariates that maintained a $p \leq 0.05$ were retained in the model. Results: The analysis 1,262,698 medications ordered. Presence on the ISMP List was associated with 1.8 times higher odds of a medication order being voided in univariate analyses ($p < 0.001$). However, when other variables were included in the model, the association between ISMP List medications being voided became non-significant with 1.008 higher odds ($p = 0.809$). Other covariates that were associated with medication orders being voided included IV fluid (OR = 0.584; $p < 0.001$), and categorizations as an anticoagulant (OR = 0.462; $p < 0.001$), benzodiazepine (OR = 0.433; $p < 0.001$), opioid (OR = 1.13; $p = 0.004$), or vaccine (OR = 0.177; $p < 0.001$). Prescriber type, location, and shift were also significantly associated with voided medication orders. Conclusion: Presence of drug on the ISMP List was not associated with voided medication orders, when controlled for other factors. However, several other factors were associated with voided medication orders. These factors will be explored further in subsequent analyses to determine their potential role in influencing medication order voiding practices.

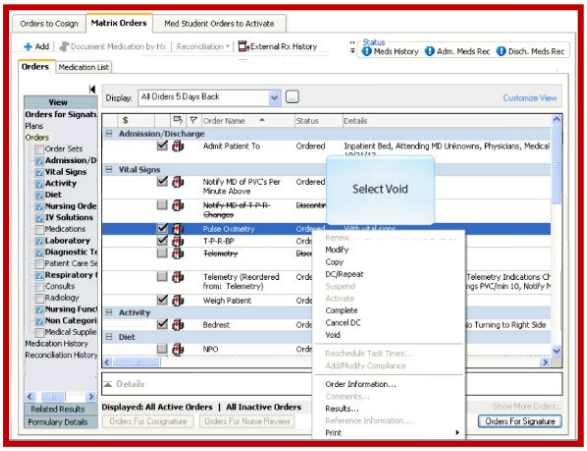
IMPLEMENTATION PRODUCTS

As part of this research, we developed educational modules to increase awareness and training on the void ordering function for clinicians. This is now part of the training process for all new clinicians.

Void Training Modules in EHR/CPOE system







Void Training: Job Aid in EHR System

FYI

University of Illinois Hospital & Health Sciences System
IS Training

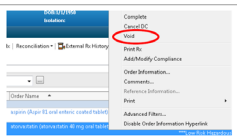
Using VOID to cancel Medication Errors

Audience: Ordering Clinicians

Best Practice: Using *VOID* to cancel medication orders that are thought to be errors.

Using "VOID" To Cancel Erroneous Medication Orders

When cancelling orders in CERNER® there are 3 options; Cancel DC, Complete and VOID. VOID is meant to be used to distinguish orders that are being cancelled due to a medication error versus other reasons. Using VOID can allow pharmacy safety experts at UI Health to learn more about medication errors. Medication errors are very common and this information is not used to single out anyone who may place an order in error, but rather to learn about why errors occur and how to prevent them. You should use VOID for you own errors or those made by others.

1. When you choose to cancel a medication order which you feel is an error, right click and select VOID.	
2. You are now asked to select the reason that you are voiding it. If one of the reasons appears appropriate, select this reason.	
3. If no reason is appropriate, please enter the free text reason that describes the error.	
4. Sign the VOID	

For additional assistance, please visit our SharePoint Site: http://intranet.uimcc.uic.edu/ISTraining/SitePages/Home.aspx.

PUBLICATIONS

Pfeifer, E., Lozovatsky, M., **Abraham, J.** & Kannampallil. T.G. (2020). Effect of an Alternative Newborn Naming Strategy on Wrong-Patient Errors: A Quasi-Experimental Study, *Applied Clinical Informatics*, 11(2):235-241.

Abraham, J., Kitsiou, S., Meng, A., Burton, S., Vatani, H. & Kannampallil T.G. (*In Press*). Effects of CPOE-based Medication Ordering on Outcomes: An Overview of Systematic Reviews, *BMJ Quality & Safety*.

Abraham, J., Ihianle, I., Choudhari, R., Jarman, A., Kannampallil, T., Galanter, W. (2018). Clinician Perspectives on Duplicate Medication Ordering Errors. *Proceedings of AMIA Annual Symposium* 2018, San Francisco, CA.

Abraham, J., Galanter, W., Touchette, D., Xia, Y., Holzer, K., Leung, V., Kannampallil, T. (in Press). Risk Factors Associated with Medication Ordering Errors. *Journal of American Medical Informatics Association.*

Under Review and Planned Submissions

King, C.R., Abraham, J., Fritz, B., Cui, Z., Galanter, W., Chen, Y., Kannampallil, T. (*under Review*). Machine learning-based Prediction of Self-Intercepted Medication Ordering Errors.

Touchette, D., Galanter, W., Kannampallil, T., Abraham, J. (*under Preparation*). Analysis of High-Risk Medications among Medication Ordering Errors.

Abraham, J., Galanter, W., Touchette, D., Kannampallil, T. (*under Preparation*). Towards a Conceptual Model for Understanding Medication Ordering Error Identification and Recovery.

Abraham, J., Galanter, W., Kannampallil, T. (*under Preparation*). Exploring Clinician Perceptions about Void, Cancel and Discontinue Orders in the CPOE system.

OTHER ACHIEVEMENTS

PI recognized as a National CPOE Expert: PI (Abraham) serves on a five-member National Leapfrog Expert panel (with David Bates, David Classen, Diane Seger, and Chris Longhurst) to establish national CPOE standards and medication safety practices.

Extension of this AHRQ R21*:* Learning and Intelligent FEedback for Safety and Vigilance in Error Reporting (LIFESAVER) AHRQ R01 (FOA: 18-795; Submission during October 2020): Medication ordering errors are one of the root contributors to adverse drug events. Such errors are underreported and minimally-explored, and consequently mitigation strategies to address their associated risk factors are limited. We propose to develop an integrated medication safety feedback framework that integrates an error reporting and exchange infrastructure for evaluating the characteristics and risk factors associated with these errors, and a personalized medication safety dashboard for delivering evidence-based strategies to foster learning from errors.